Appendix to Specification Amendments

Examples of other small molecules useful in the invention can be found in Komoriya et al. ("The Minimal Essential Sequence for a Major Cell Type-Specific Adhesion Site (CS1) Within the Alternatively Spliced Type III Connecting Segment Domain of Fibronectin Is Leucine-Aspartic Acid-Valine", J. Biol. Chem., 266 (23), pp. 15075-79 (1991)). They identified the minimum active amino acid sequence necessary to bind VLA-4 and synthesized a variety of overlapping peptides based on the amino acid sequence of the CS-1 region (the VLA-4 binding domain) of a particular species of fibronectin. They identified an 8-amino acid peptide, Glu-Ile-Leu-Asp-Val-Pro-Ser-Thr (SEQ ID NO: 5), as well as two smaller overlapping pentapeptides, Glu-Ile-Leu-Asp-Val (SEQ ID NO: 6) and Leu-Asp-Val-Pro-Ser (SEQ ID NO: 7), that possessed inhibitory activity against fibronectin-dependent cell adhesion. Certain larger peptides containing the LDV sequence were subsequently shown to be active in vivo (T.A. Ferguson et al., "Two Integrin Binding Peptides Abrogate T-cell-Mediated Immune Responses In Vivo", Proc. Natl. Acad. Sci. USA, 88, pp. 8072-76 (1991); and S. M. Wahl et al., "Synthetic Fibronectin Peptides Suppress Arthritis in Rats by Interrupting Leukocyte Adhesion and Recruitment", J. Clin. Invest., 94, pp. 655-62 (1994)). A cyclic pentapeptide, Arg-Cys-Asp-TPro-Cys (SEQ ID NO: 8) (wherein TPro denotes 4-thioproline), which can inhibit both VLA-4 and VLA-5 adhesion to fibronectin has also been described. (See, e.g., D.M. Nowlin et al., "A Novel Cyclic Pentapeptide Inhibits Alpha4Beta1 Integrin-mediated Cell Adhesion", J. Biol, Chem., 268(27), pp. 20352-59 (1993); and PCT publication PCT/US91/04862). This pentapeptide was based on the tripeptide sequence Arg-Gly-Asp from FN which had been

known as a common motif in the recognition site for several extracellular-matrix proteins.